

I. AMENDMENTS TO THE SPECIFICATION

Please replace the first paragraph on page 1 with the following amended paragraph:

-- This application is a continuation of U.S. Patent Application Serial No. 09/781,076, filed February 8, 2001, now U.S. Patent No. 6,716,449, issued April 6, 2004, which claims priority from U.S. Provisional Application Serial No. 60/181,358, filed February 8, 2000, the disclosures of which are hereby incorporated by reference in their entireties.--

Please replace the second paragraph on page 3, lines 10-18, with the following amended paragraph:

--In certain preferred embodiments, the present invention comprises a controlled release dosage form that delivers an opioid agonist and an opioid antagonist over an extended period of time. In these oral embodiments, the dosage form includes an amount of an opioid agonist, preferably a ~~biomedically acting~~ bimodally-acting opioid agonist, and an amount of an opioid antagonist, and upon administration the dosage form delivers an analgesic or sub-analgesic amount of the opioid agonist over the dosing interval, along with an amount of the opioid antagonist effective to enhance the analgesic potency of the opioid agonist and attenuate the anti-analgesia, hyperalgesia, hyperexcitability, physical dependence and/or tolerance effects of the opioid agonist. --

Please replace the fourth paragraph on page 3, lines 26-27, with the following amended paragraph:

--The present invention is also directed to the use of the above-mentioned controlled release formulations for maintenance treatment of previously detoxified opiate addicts. --

Please replace the sentence beginning at line 21 on page 7 with the following amended sentence:

- -When the controlled release dosage form comprises a transdermal delivery system, ~~The~~ the rate of delivery of the opioid agonist will be such that a sufficient mean relative release rate (or flux rate) of the opioid agonist contained in the dosage form is delivered from the transdermal dosage form upon administration.- -

Please replace the sentence beginning at line 17 on page 8 with the following amended sentence:

- -This is because the excitatory opioid receptor antagonists may enhance the analgesic effects of the ~~opioid~~ opioid agonists by attenuating the anti-analgesic excitatory side effects of the opioid agonists.- -

Please replace the sentence beginning at line 23 on page 10 with the following amended sentence:

- -The excitatory opioid receptor antagonists of the invention are preferably selected from the group consisting of naloxone, naltrexone, diprenorphine, etorphine, dihydroetorphine, pharmaceutically acceptable salts thereof and mixtures thereof. - -

Please replace the paragraph, beginning at line 34 on page 16 with the following amended paragraph:

- -The controlled release dosage form can be a transdermal patch comprising:
(a) a backing layer which is substantially impervious to said opioid agonist and opioid antagonist; and (b) a polymer matrix layer which is adhered to said backing layer and which has

dispersed therein said opioid agonist and opioid, said polymer being bioacceptable and permitting said opioid agonist and opioid antagonist to be transmitted for transdermal absorption, said opioid agonist and opioid antagonist being stable in said polymer matrix. - -

Please replace the sentence beginning at line 31 on page 35 with the following amended sentence:

- -In certain embodiments, the oral dosage form contains up to 60% (by weight) of at least one polyalkylene glycol as part of the controlled release matrix. - -

Please replace the abstract on page 74 with the following amended abstract:

- -Controlled-release dosage forms containing an opioid agonist; an opioid antagonist; and a controlled release material release during a dosing interval an analgesic or sub-analgesic amount of the opioid agonist along with an amount of said the opioid antagonist effective to attenuate a side effect of said the opioid agonist. The dosage form provides analgesia for at least about 8 hours when administered to human patients. In other embodiments, the dose of antagonist released during the dosing interval enhances the analgesic potency of the opioid agonist.